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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,532	10/07/2004	Gerd Ascher	KS4255US (#90711)	8872

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D. Peter Hochberg, Esq.
D. Peter Hochberg, Co., L.P.A.
1940 East 6th Street - 6th Floor
Cleveland, OH 44114

EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
01/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,532	ASCHER ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicants have cancelled claims 1-2 and have amended claims 5-7 to overcome the 35 USC 101 and 112 rejections over those claims. The rejections are hereby withdrawn.

Applicants have argued over the 35 USC 112, second paragraph rejection over claim 5 that one of skill in the art is aware what a pleuromutilin is and therefore should not be considered indefinite.

This argument is not found to be persuasive. Looking at claim, one would determine that at the 14 position there is a methoxy group; however, it is evident from claim 6 that this is not the case and that there are substituents added to that position. Though the basic structure of a pleuromutilin may be what is given in claim 5, one would not determine that Applicants intend for a substituent to be added to the O group on position 14 of the ring structure. Accordingly, the rejection is maintained.

Applicants have argued over the 35 USC 112, first paragraph rejection that experimental results are presented in which pleuromutilins inhibit the activity of 5 different Helicobacter pylori strains. Applicants further point out that the pleuromutilins show activity against strains that are metronidazole-resistant. Applicants assert that it is evident that compounds that influence activity of Helicobacter pylori contribute to the treatment of diseases which are mediated by Helicobacter pylori.

In response to the above arguments, it is noted that present claim 3 broadly reads on a method for the treatment of diseases mediated by Helicobacter pylori. There

are many diseases associated with Helicobacter pylori (as evidenced by Applicants own admission in the specification) including active chronic gastritis, chronic renal failure and HIV to name a few. Applicants make a comparison between metronidazole and tetracycline and assert that they are treatments for diseases mediated by Helicobacter pylori and that because they show in vitro activity against Helicobacter pylori, it would make sense that pleuromutilins would also be an effective treatment for diseases mediated by Helicobacter pylori because they are effective in the same in vitro assays. The arguments are not found persuasive because there are many diseases that are associated with Helicobacter pylori and every disease is not treated by every compound that shows inhibitory activity against Helicobacter pylori. Given the logic pattern that Applicant has presented, any agent that shows activity against Helicobacter pylori would treat any disease mediated by Helicobacter pylori, including renal failure and HIV. There is no indication within the literature that compounds that are know to be effective against Helicobacter pylori, such as metronidazole, are effective treatments for HIV or renal failure. Therefore, it cannot be assumed that because a compound is effective in an in vitro assay, that it will automatically treat any disease mediated by that particular organism. Therefore, the rejection is maintained and is given below for Applicant's convenience.

The rejections are modified due to Applicants cancellation of claims.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 5 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, within the structure given in the claim, the "O" at the 14 position of the ring structure does not have a substituent indicating the addition of a group. Claim 6 further limits claim 5, and the "O" at the 14 position is connected to a group or formula. Applicant is directed to complete claim 5 by putting another "R" group to exemplify the invention. For the sake of compact prosecution, the claim is being read with the "O" at the 14 position being open to contain any group or formula.

Claims 3-7 rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for treating diseases mediated by Helicobacter pylori, and in particular chronic gastritis. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as

the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPTQ 546.

1) The nature of the invention and breadth of the claims: The nature of the invention and breadth of the claims is drawn to a method for the treatment of diseases mediated by Helicobacter pylori (chronic gastritis is the elected species) comprising administration of an effective amount of a pleuromutilin.

2) The presence or absence of working examples and the amount of direction or guidance presented: The determination of a particular claimed compound in the treatment of diseases mediated by Helicobacter pylori, and in particular chronic gastritis, requires the synthesis of the compound, formulation in a suitable dosage form, and testing in a known assay that is correlated with clinical efficacy. The only examples presented by Applicant in the specification are in vitro tests showing that I-Valnemulin has an effect on H. pylori (pages 55-56). There is no data in accepted models of chronic gastritis suggesting that these compounds would show clinical efficacy in treating this disease.

The issue in *Ex parte Balzarini* 21 USPQ2d 1892 concerned HIV treatment and the Board of Patent Appeals and Interferences wrote "while the *in vitro* testing performed on these anti-viral compound appears to be useful as a screening tool in order to determine which of these anti-viral compounds are candidates for further

testing to determine if they possess *in vivo* utility, the *in vitro* tests were not predictive of *in vivo* efficacy". Furthermore, the issue in *Fujikawa v. Wattanasin* 39 USPQ2d 1895 was adequacy of *in vitro* testing of inhibitors of cholesterol biosynthesis and U.S. Court of Appeals Federal Circuit wrote, "*in vitro* results, in combination with a known correlation between such *in vitro* results and *in vivo* activity, may be sufficient to establish practical utility". A working example in *in vivo* experiments showing that the compounds would effectively treat the claimed diseases is lacking.

3) The state of the prior art: The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., Chiron Corp. v. Genentech Inc., 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004).

A review article by Malfertheiner et al. (Aliment Pharmacol Ther 2002: 16: 167-180) points out therapies for the management of Helicobacter pylori. Beginning on page 173, Malfertheiner et al. discusses therapy and management which include proton pump inhibitors and ranitidine bismuth, among other treatment regimens. However there is no mention of treatment with valnemulin or any pleuromutilin.

Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual" or not provided in the specification, *Ex parte Jovanovics*, 211 USPQ 907, *In re Langer*, 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 200 USPQ 925 concerning the type of testing needed to support *in vivo* use claims. Also see MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

4) The quantity of experimentation necessary: "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed Cir. 1993)". Undue experimentation would be required in order to practice Applicant's invention because there are no examples provided in the specification. One would have to determine a useful model that correlates with clinical efficacy, a dosage range would need to be determined as well as a route of administration. Further, if any of the above failed, then the artisan would have to start over again in an effort to determine the suitable methods, dosage ranges and routes of administration in which to determine if the compounds will work to treat chronic gastritis.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is (571)272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617